UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/588,359	08/03/2006	Moon-Hee Sung	4240-147	5092

23448 7590 07/18/2008

INTELLECTUAL PROPERTY / TECHNOLOGY LAW
PO BOX 14329
RESEARCH TRIANGLE PARK, NC 27709

EXAMINER	
BLUMEL, BENJAMIN P	
ART UNIT	PAPER NUMBER
1648	

MAIL DATE	DELIVERY MODE
07/18/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/588,359	SUNG ET AL.	
	Examiner	Art Unit	
	BENJAMIN P. BLUMEL	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *10,11 and 15-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,12-14 and 18-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *8/3/06* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/3/06 & 9/15/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of the required species in the reply filed on April 25, 2008 is acknowledged. The traversal is on the ground(s) that given the related nature of the claimed pgs genes/vectors; the fact that the claimed microorganisms of claim 4 have a special technical feature of presenting low toxicity *in vivo*; the various forms of capsid antigen are related since they all represent similar forms of such a protein; and the various modes of administration also share a special technical feature because they are involved in the delivery of a substance to a subject. This is not found persuasive because the microorganisms of claim 4, the forms of capsid protein and the modes of administration, while having some similar feature or purpose, are distinct since they are very different bacteria, particularly *M. bovis* is an intracellular bacteria, while *E. coli* is not; the forms of the capsid proteins require different searches since they require different steps in order to obtain the claimed protein; and the modes of administration would also require different searches since oral administration is usually intended for substances that can't be effected by stomach acids while celiac (abdominal) injections are reserved for other forms of compounds. However, upon further consideration, the species election for groups **A.** and **B.** have been withdrawn.

The requirement is still deemed proper and is therefore made FINAL.

Claims 10, 11 and 15-17 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on April 25, 2008.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 2 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claimed invention is drawn to the vectors pHCE2LB:pgsA:CVP2-1, pHCE2LB:pgsA:VP2-2 or pHCE2LB:pgsA:VP2.

It is apparent that the claimed vectors are required to practice the claimed invention because they are a necessary limitation for the success of the invention as stated in the claims. As a required element it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If it is not so obtainable or available, the enablement requirements of 35 U.S.C. § 112, first paragraph, may be satisfied by a deposit of the claimed vectors. See 37 CFR 1.802. Therefore, access to the claimed vectors is required to practice the invention. The specification does not provide a repeatable method for making the claimed vectors without access to these vectors and it does not appear to be readily available material.

Deposit of the claimed vectors in a recognized deposit facility would satisfy the enablement requirements of 35 U.S.C. 112., because the strains would be readily available to the public to practice the invention claimed, see 37 CFR 1.801- 37 CFR 1.809.

If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 CFR 1.808.

If a deposit is not made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such

assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made at an acceptable depository and that the following criteria have been met:
(a) during the pendency of this application, access to the invention will be afforded to one determined by the Commissioner to be entitled thereto;
(b) all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon granting of the patent;
(c) the deposit will be maintained for a term of at least thirty (30) years and at least five (5) years after the most recent request for the furnishing of a sample of the deposited material;
(d) a viability statement in accordance with the provisions of 37 CFR 1.807; and
(e) the deposit will be replaced should it become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification.

In addition the identifying information set forth in 37 CFR 1.809(d) should be added to the specification. See 37 CFR 1.803 - 37 CFR 1.809 for additional explanation of these requirements.

Claims 7-9, 12 and 18-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition that induces an immune response in mice to canine parvovirus capsid protein VP2, does not reasonably provide enablement for a vaccine that can prevent parvovirus infections. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Nature of the invention/Breadth of the claims. The claims are drawn to a vaccine for the prevention of parvovirus infections, such as canine parvovirus infections and feline panleukopenia (FPV). The vaccine contains lactic-acid bacteria that express a VP2 capsid protein of parvovirus on its surface. The vaccine is administered orally. The claimed invention also includes a feedstuff additive for the prevention of parvovirus that contains these recombinant bacteria.

State of the prior art/Predictability of the art. The art does not recognize a vaccine that can prevent parvovirus infections. For example, Rose et al. tested the effectiveness of three commercially available porcine parvovirus vaccines (PPV), which contained inactivated PPV. However, even though these vaccines were employed, Rose et al. still observed viral load in infected sows and offspring following challenge. (See pages 134, 136 and 137). Patterson et al. (JAVMA, 2007) reported that only 31% of felines receiving an inactivated feline panleukopenia virus as a vaccine had protective titers. (See XXXX). Furthermore, Decaro et al. (The new Microbiologica, 2008) report that vaccination of canines against canine parvovirus type 2 (CPV-2) failed as several dogs in community kennels were infected with CPV type 2c (CPV-2c). (See XXXX).

W*orking examples.* One working example exists relating to *in vivo* usage of recombinant *Lactobacillus casei* expressing canine parvovirus VP2-2 and VP2-1 on the surface. These recombinant bacteria were used to produce reactive antibodies in mice. However, the inoculated mice were not challenged with a virulent strain of CPV, nor were the reactive antibodies tested for at least *in vitro* neutralization activity. In addition, even though reactive antibodies were isolated from inoculated mice, it is unclear what portion of these antibodies were capable of neutralizing infectious CPV virus, since antibodies may be reactive, but not capable of stopping CPV virus from infecting target cells.

Amount of experimentation necessary. Additional research is required in order to determine how effective a vaccine only containing recombinant lactic-acid bacteria that express parvovirus VP2 on its surface or any composition for that matter, is at preventing parvovirus

infections, particularly, CPV and FPV since the only recognized vaccines are inactivated forms of such viruses, but even these vaccines do not prevent parvovirus infections.

For the reasons discussed above, it would require undue experimentation for one skilled in the art to use the claimed methods.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3-6, 13 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sung et al. (US PGPub 2004/0253704 A1) in view of Lopez de Turiso et al. (The Journal of General Virology, 1991).

The claimed invention is drawn to a recombinant lactic acid bacterium that expresses the parvovirus capsid VP2 protein along with the pgsA gene. The capsid protein is expressed on the surface of the bacteria during the culturing of the recombinant bacteria.

Sung et al. teach the expression of viral antigens when recombinant *Lactobacillus casei* bacteria (a lactic acid bacteria) contained the vector pHCE1LB with Hepatitis B antigen coding regions and genes for pgsA, pgsB and/or pgsC. The expression construct thereby expresses these proteins on the surface of the bacteria. However, Sung et al. do not teach expressing parvovirus capsid VP2 antigens. *See paragraphs 58, 60, 64-70, 150, 171 and 204.*

Lopez et al. teach the use of *E. coli* to express whole length canine parvovirus VP2 antigens as part of an expression cassette. *See page 2446.*

It would have been obvious to one of ordinary skill in the art to modify the composition taught by Sung et al. in order to generate a recombinant *Lactobacillus* that contains an expression vector encoding pgsA and parvovirus capsid VP2 protein. One would have been motivated to do so, given the suggestion by Sung et al. that the bacterium be used to express antigens of interest. There would have been a reasonable expectation of success, given the knowledge that parvovirus capsid VP2 proteins can be expressed by bacteria through an expression vector/plasmid, as taught by Lopez de Turiso et al. Thus the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 1-6, 13 and 14 are rejected under 35 U.S.C. 103(a) as being obvious over Sung et al. (US 2005/0249752 A1) in view of Lopez de Turiso et al. (The Journal of General Virology, 1991).

One of the applied references has common inventors with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing

under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

The claimed invention is drawn to a recombinant *Lactobacillus casei* that expresses the VP2 capsid protein of a parvovirus along with the pgsA gene in the plasmid pHCE2LB resulting in the construct pHCE2LB:pgsA:VP2. The capsid protein is expressed on the surface of the bacteria through the culturing of the recombinant bacteria.

Sung et al. teach the development of recombinant *Lactobacillus casei* bacteria that expressed Human Papillomavirus antigens inserted into a pHCE2LB vector which also expresses pgsA, pgsB and/or pgsC. Based on the teachings of Sung et al. and the specification of the instant application, the recombinant bacterial-vector systems are the same. However, Sung et al. do not teach expressing parvovirus capsid VP2 proteins in place of the HPV antigens. *See paragraphs 7, 8, 18-23, 31 and examples 1 and 2.*

Lopez et al. teach the use of *E.. coli* to express whole length canine parvovirus VP2 antigens as part of an expression cassette. *See page 2446.*

It would have been obvious to one of ordinary skill in the art to modify the composition taught by Sung et al. in order to generating a recombinant *Lactobacillus casei* that contains the pHCE2LB:pgsA:VP2 vector. One would have been motivated to do so, given the suggestion by Sung et al. that the bacterium be used to express antigens of interest. There would have been a reasonable expectation of success, given the knowledge that a canine parvovirus VP2 capsid antigen can be expressed by bacteria through an expression vector/plasmid, as taught by Lopez de Turiso et al. Thus the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15. Furthermore, the foreign priority papers have not been filed as of the date of this Office action.

Claim Objections

Claims 7 and 18-20 are objected to because of the following informalities: these claims recite, "...prevention of parvovirus...", however it is suggested to amend the claims to recite, "...prevention of parvovirus infection...", since a vaccine is being claimed. Appropriate correction is required.

Summary

No claims are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BENJAMIN P. BLUMEL whose telephone number is (571)272-4960. The examiner can normally be reached on M-F, 8-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-1600. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Stacy B Chen/
Primary Examiner, Art Unit 1648

/BENJAMIN P BLUMEL/
Examiner
Art Unit 1648